From skin biopsy to neurons through a pluripotent intermediate under good manufacturing practice protocols.

Journal: Stem Cells Transl Med

Publication Year: 2012

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PubMed link: 23197638

Funding Grants: Generation of Pluripotent Cell Lines from Human Embryos, Generation of clinical grade human iPS cells, In vitro reprogramming of mouse and human somatic cells to an embryonic state, CIRM Shared Research Laboratories

Public Summary:
The clinical application of human-induced pluripotent stem cells (hiPSCs) requires not only the production of Good Manufacturing Practice-grade (GMP-grade) hiPSCs but also the derivation of specified cell types for transplantation under GMP conditions. Previous reports have suggested that hiPSCs can be produced in the absence of animal-derived reagents (xenobiotics) to ease the transition to production under GMP standards. However, to facilitate the use of hiPSCs in cell-based therapeutics, their progeny should be produced not only in the absence of xenobiotics but also under GMP conditions requiring extensive standardization of protocols, documentation, and reproducibility of methods and product. Here, we present a successful framework to produce GMP-grade derivatives of hiPSCs that are free of xenobiotic exposure from the collection of patient fibroblasts, through reprogramming, maintenance of hiPSCs, identification of reprogramming vector integration sites (nrLAM-PCR), and finally specification and terminal differentiation of clinically relevant cells. Furthermore, we developed a primary set of Standard Operating Procedures for the GMP-grade derivation and differentiation of these cells as a resource to facilitate widespread adoption of these practices.

Scientific Abstract:
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